3. Claim objection

The Examiner objected to claim 5 because it allegedly contains a method step with in a product claim. Applicants disagree with the Examiner's interpretation and note that the "wherein" on line 3 of the claim modifies each of the following lines. Nevertheless, Applicants have added the word "wherein" at line 6 as suggested by the Examiner. Accordingly, Applicants request withdrawal of the objection.

4. Rejections under 35 U.S.C. § 112

a. Written description rejection over scope of polynucleotides claimed

Claims 5, 9-18 and 34-40 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not fulfilling the written description requirement. Applicants respectfully traverse the rejection.

With regard to claims 5 and 9-18, the Examiner argued that all polynucleotides encoding sequences at least 70% identical to SEQ ID NO:2 were not described in the specification. While Applicants strongly disagree with the Examiner, to expedite prosecution Applicants have introduced the limitations of claim 6 into claim 5, thereby rendering the rejection moot.

With regard to claims 34-40, the Examiner argued that the application fails to describe a polynucleotide comprising at least 200 contiguous nucleotides of SEQ ID NO:1. Relying on the Federal Circuit decision, *Fiers v. Ravel*, the Examiner argued that a description of the "DNA itself" was required to provide an adequate description. *See*, Office Action, page 4. The Examiner argues that it is unclear from the specification that the Applicant was in possession of the full scope of the claimed invention because the application "only presents a statement for any such polynucleotide being at least 65% identical to said fragments." *See*, Office Action, page 4.

The Examiner appears to misinterpret the statement in *Fiers*. The claims in question meet all of the requirements set forth by the Federal Circuit, including those set forth in *Fiers*. The *Fiers* case involved an application that lacked any nucleotide

sequence for a claimed gene. In contrast to the facts in *Fiers*, the present application provides a nucleotide sequence. The present claims recite a specific sequence (SEQ ID NO:1). The claims at issue encompass sequences at least 65% identical to 200 contiguous nucleotides of SEQ ID NO:1. Any and all of the sequences encompassed by the claims can be readily determined by those of skill in the art. The court in *Fiers* specifically stated that "a conception of a DNA requires a precise definition, such as by structure, **formula**, chemical name, or physical properties" [emphasis added]. *See Fiers*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). Claim 34 effectively sets forth a formula for determining the sequences encompassed by the claims. Unlike the sequences involved in *Fiers*, each and every sequence encompassed by the claim could be written out by one of skill in the art with only the specification as a reference. That was not the case in *Fiers*.

Applicants note that the sequences recited in claim 34 are easy to select and generate. The Examiner has not explained any reason for why those of skill in the art would doubt that the sequences encompassed by the claim would not have been in possession of the inventors. The question is not whether the inventors had physical possession of each sequence encompassed, but rather whether each sequence could be envisioned. As discussed above, it would be a simple, if tedious matter, to generate each and every sequence encompassed by the claims.

Applicants note that the Examiner rejected claim 35 even though the claim encompasses sequences that are **identical** to at least 200 contiguous nucleotides of SEQ ID NO:1. Applicants invite the Examiner to explain why those of skill in the art would not understand that the inventors were in possession of sequences encompassing at least 200 contiguous nucleotides of SEQ ID NO:1 when SEQ ID NO:1 and fragments thereof are specifically described in the specification. *See, e.g.*, page 17, lines 1-5 and page 18, lines 13-14 of the specification.

In light of the above discussion, Applicants respectfully request withdrawal of the rejections.

b. Rejection of claim 12

Claim 12 was rejected under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification. Applicants traverse the rejection. However, to expedite prosecution, Applicants have canceled claim 12, thereby rendering the rejection moot.

c. Enablement rejection of claims 20-28 and 30

The Examiner rejected claims 20-28 as allegedly not enabled for the full scope of the claims. Specifically, the Examiner argued that while the claims were enabled for methods of delaying fruit dehiscence in Arabidopsis, the specification allegedly did not enable a method of delaying fruit dehiscence in any plant. The Examiner's rejection is based in part on Quattrocchio *et al.*, which the Examiner states teaches that heterologous bHLH transcription factors do not predictably function as they do in homologous plants. *See*, Office Action, page 6. In light of Quattrocchio *et al.*, the Examiner concludes that "it is reasonable to infer that co-suppression with a heterologous polynucleotide encoding a heterologous bHLH transcription factor will not predictably function either." *See*, Office Action, page 6. In addition, regarding antisense constructs, the Examiner argues that "the use of antisense constructs was not routine in the art at the time of the Applicant's invention" and was mainly used to suppress expression of homologous expression. *See*, Office Action, page 6. Applicants respectfully traverse the rejection.

The Examiner has not set forth a *prima facie* enablement rejection regarding either co-suppression (commonly referred to as RNA interference or RNAi) or antisense suppression of *IND1* expression. For example, the Examiner argues that Quattrocchio *et al.* provides evidence that the effect of expression of heterologous bHLH genes in plants is unpredictable and therefore, the effect of co-suppression using heterologous polynucleotides is also unpredictable. As argued previously, the citation of Quattrocchio *et al.* is irrelevant because the reference describes ectopic expression of bHLH transcription factors not suppression of expression of the IND1 transcription factor.

Moreover, Applicants previously submitted a Declaration of Dr. Johan Botterman, Ph.D. which demonstrates that co-suppression of IND1 using either homologous Arabidopsis sequences **or heterologous Brassica sequences** resulted in inhibition of fruit dehiscence. The declaration provides evidence that is in stark contrast to the Examiner's statement that co-suppression with heterologous sequences is unpredictable. Thus, even if the Examiner has set forth a *prima facie* rejection, the evidence in the declaration rebuts the rejection. Indeed, the evidence in the declaration is directly on point regarding co-suppression of the particular gene in the claims, unlike the Quattrocchio *et al.* reference, which at best describes ectopic expression (not co-suppression) of bHLH polynucleotides unrelated to those recited in the present claims. Thus, sense orientation constructs encompassed in the claims and their use to suppress *IND1* expression are fully enabled by the specification.

Regarding antisense constructs, Applicants strongly disagree with the Examiner's statement that "the use of antisense constructs was not routine in the art at the time of the Applicant's invention." *See*, Office Action, page 6. As noted in the previous Amendment, "plant molecular biologists commonly use antisense technology to reduce expression of gene expression. While such technology often requires screening of transformants to select plants with a desired phenotype, the screening is a routine part of laboratory work. In no way does the screening amount to undue experimentation." *See*, Amendment filed October 8, 2002, page 10.

As further evidence to rebut the Examiner's statement, Applicant's note that the patent office has issued patents claiming the use of antisense technology in plants since at least 1992, **eight years** before the filing date of the present application. *See, e.g.*, U.S. Patent No. 5,107,065. Applicants remind that Examiner that issued claims are presumed valid and thus enabled. Indeed, a search of abstracts in the US patent office website using the keywords "antisense" and "plant" reveals at least thirty patents issued before the present application's filing date.

Moreover, Applicants note that the claims need not involve use of heterologous antisense sequences to inhibit IND1 expression. For example, the two

Brassica IND1 sequences described in the previously filed Declaration of Martin F. Yanofsky, Ph.D. are approximately 75% identical to SEQ ID NO:2. Thus, the present claims encompass use of endogenous Brassica sequences that are at least 65% identical to SEQ ID NO:1 to inhibit expression of Brassica IND1 sequences.

Furthermore, those of skill would have recognized the advantage of using antisense sequences that are highly homologous to the endogenous IND1 sequence of any particular plant. Indeed, the present application also teaches the advantages of using substantially identical sequences to inhibit expression using antisense sequences. *See, e.g.*, page 16, lines 23-30 of the present application. Thus, in fact, those of skill in the art are not left with a random set of possible antisense sequences from which to select. Instead, based on both knowledge in the art and teachings in the specification, those of skill in the art would select a few sequences that are related to an *IND1* sequence of interest and those few sequences would be tested for activity. It is improper for the Examiner to suggest that a particularly large number of sequences would be tested to identify inhibitory sequences.

In light of the above arguments, Applicants respectfully request withdrawal of the rejections of claims 20-28 and 30.

Regarding new claims 41 and 43, Applicants note that the Declaration of Dr. Johan Botterman, Ph.D. is particularly relevant. The evidence discussed in the Botterman Declaration demonstrates that Brassica sequences in particular are effective in suppression of IND1 expression in Arabidopsis. Thus, there is every reason to expect that heterologous sequences (e.g., Arabidopsis sequences) are effective to suppress Brassica IND1 expression.

d. Rejection of claims 34-40

Claims 34-40 were rejected as allegedly not enabled for the full scope of the claims. Specifically, the Examiner argued that while the application teaches how to co-suppress expression of IND1 using SEQ ID NO:1, the application does not teach how to make or use the claimed expression cassette to delay fruit dehiscence. The Examiner

argues that it would require undue experimentation to screen through fragments at least 65% identical to any 200 base pair fragment of SEQ ID NO:1 to identify those that suppress IND1 expression in a plant. Applicants respectfully traverse the rejection.

To establish a *prima facie* case of non-enablement, the Examiner must show that undue experimentation would be required to make and use the claimed invention. Even if the practice of the claimed invention requires a considerable amount of experimentation, it is not necessarily "undue" experimentation:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or it the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) (citing *In re Angstadt*, 190 USPQ 214 (CCPA 1976).
> MPEP § 2164.06.

In contrast to the statements in the Office Action, the present application provides more than merely an instruction to screen a large number of sequences at least 65% identical to SEQ ID NO:1 in hope that a sequence will inhibit expression. The specification specifically teaches that it is desirable to select sequences that are at least similar and preferably highly similar or identical to at least a portion of the endogenous sequence to be inhibited (e.g., the endogenous IND1 gene). The paragraph spanning pages 17-18 of the application states:

> The introduced sequence generally will be substantially identical to the endogenous sequence intended to be repressed. This minimal identity will typically be greater than about 65%, but a higher identity might exert a more effective repression of expression of the endogenous sequences. Substantially greater identity of more than about 80% is preferred, though about 95% to absolute identity would be most preferred.

Thus, the amount of screening to identify an inhibiting sequence is likely to be quite limited. Those of skill in the art would know not to merely design every sequence at least 65% identical to SEQ ID NO:1 and to then screen them all. Instead, sequences very similar to the endogenous plant sequence would be selected and screened.

The small number of sequences that would be screened to identify an optimum inhibitory sequence does not amount to undue experimentation. Accordingly, Applicants respectfully request withdrawal of the rejection.

Moreover, the Examiner appears to argue that those of skill would have difficulty in identifying sequences at least 65% identical to a 200 base pair sequence of SEQ ID NO:1 to inhibit IND1 expression. The Examiner's rejection is apparently premised on the possibility that similar but not identical sequence may not inhibit IND1 expression. Applicants note that claim 35 is limited to fragments of SEQ ID NO:1, not sequences at least 65% identical. Thus, it does not appear that the Examiner should have rejected claim 35 in light of the Examiner's reasoning set forth in the rejection.

*5. **Rejections under 35 U.S.C. § 103***

Claims 5-7, 9-18 and 34-40 were rejected as obvious under 35 U.S.C. § 103 over Ryan *et al.* in view of Quattrocchio *et al.* Applicants respectfully traverse the rejection.

The Examiner argued that "one of skill in the art would have recognized the Ryan sequence as encoding a plant Ra transcription factor, as taught by Ryan." This statement is not accurate. In fact, Ryan *et al.* only states that the provided sequence "contains similarity to transcriptional activator Ra," **not** that the sequence encodes a Ra transcription factor as the Examiner states. Thus, it is not clear that one of skill in the art would expect that the sequence played any particular role in plant development in light of the bare sequence and a reference to an unquantified homology to another protein provided by Ryan *et al.* Quattrocchio *et al.* does not correct this defect.

Absent any **specific** predicted or known function for the sequence, it is improper to argue that those of skill in the art would have been motivated to do **anything** with the sequence, let alone construct the claimed expression vectors. It may be true that scientists are motivated to study **any** sequence in the world to find out what it does. This, however, is not a specific motivation to construct an expression cassette from any particular sequence for which some homology has been identified.

Indeed, Applicants note that the Examiner has rejected nearly each claim depending from claims 5 and claim 34 as allegedly not enabled. What is the specific motivation of one skilled in the art to operably link the specific types of promoters (e.g., constitutive, tissue specific, dehiscence zone-specific, etc.) to the sequence of Ryan *et al.*? Without a specific motivation to make the expression cassette recited in **each** dependent claim, the Examiner has not set forth a *prima facie* rejection. To date, the Examiner has not explained why those of skill would be motivated to make any of the expression cassettes specifically recited in **any** dependent claim. Accordingly, Applicants respectfully request withdrawal of the rejections.

Finally, the Examiner's position citing the same reference (Quattrocchio *et al.*) as proving that the claimed invention is both obvious and lacking enablement is contradictory. In essence, the Examiner's argument is that one of skill would not know whether the invention works, or how to practice it, but that, if it does work and if one of skill did know how to practice it, it would be obvious. This logical non sequitur has been expressly disapproved by the Federal Circuit. *See In re Dow Chemical*, 5 USPQ2d 1529, 1531 (Fed Cir. 1988). As indicated by the Federal Circuit in *Dow*, simultaneously pursuing both arguments demonstrates substitution of a proper obviousness analysis with an "obvious to try" standard, which has been repeatedly rejected by the Board of Appeals and the Federal Circuit.

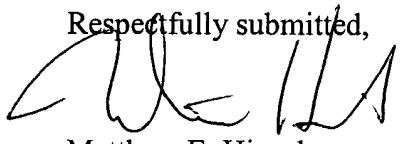
Indeed, in the enablement rejections, the Examiner repeatedly argues that the role of one transcription factor in plant development does not provide sufficient information regarding the role of a related transcription factor. Nevertheless, the Examiner argues that Quattrocchio *et al.* would motivate those of skill in the art to make the claimed expression cassette "because one of ordinary skill in the art would know that plant transcriptions factors regulate expression of plant genes and phenotypes." *See*, Office Action, page 8. Given the Examiner's position that related sequences may have very different roles and functions, how can the Examiner argue that **any** function is obvious for the Ryan *et al.* sequence, especially in light of the fact that Ryan *et al.* merely states that the sequence has some similarity to Ra, not that it is a Ra transcription factor?

The motivation the Examiner points to is merely an invitation to experiment, not a motivation to obtain any specific goal. Accordingly, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

5. (Twice Amended) An expression cassette comprising a promoter operably linked to a heterologous IND1 polynucleotide, or a complement thereof, encoding SEQ ID NO:2, [an IND1 polypeptide, wherein:

the IND1 polypeptide is at least about 70% identical to SEQ ID NO:2;

the IND1 polypeptide comprises a basic helix-loop-helix (bHLH) domain; and] wherein

introduction of the expression cassette into a plant to suppress IND1 expression results in a plant with delayed fruit dehiscence.

13. (Twice Amended) A plant comprising a recombinant expression cassette comprising a promoter operably linked to a polynucleotide encoding SEQ ID NO:2 [an IND1 polypeptide, wherein:

the IND1 polypeptide is at least about 70% identical to SEQ ID NO:2; and

the IND1 polypeptide comprises a basic helix-loop-helix (bHLH) domain].

APPENDIX B

CLAIMS PENDING WITH ENTRY OF AMENDMENTS

5. (Twice Amended) An expression cassette comprising a promoter operably linked to a heterologous IND1 polynucleotide, or a complement thereof, encoding SEQ ID NO:2, wherein introduction of the expression cassette into a plant to suppress IND1 expression results in a plant with delayed fruit dehiscence.

7. The expression cassette of claim 5, wherein the IND1 polynucleotide comprises positions from about 2765 to about 3361 of SEQ ID NO 1.

9. The expression cassette of claim 5, wherein the promoter is constitutive.

10. The expression cassette of claim 5, wherein the promoter is tissue specific.

11. The expression cassette of claim 10, wherein the promoter is a dehiscence zone specific promoter.

13. (Twice Amended) A plant comprising a recombinant expression cassette comprising a promoter operably linked to a polynucleotide encoding SEQ ID NO:2.

14. (Amended) The plant of claim 13, wherein the polynucleotide encoding the IND1 polypeptide is operably linked to the promoter in the antisense orientation.

15. (Amended) The plant of claim 13, wherein the polynucleotide encoding the IND1 polypeptide is operably linked to the promoter in the sense orientation.

16. (Amended) The plant of claim 15, wherein the polynucleotide sequence further comprises a second polynucleotide sequence encoding the IND1 polypeptide wherein the second polynucleotide is operably linked to a second promoter in the antisense orientation.

17. The plant of claim 13, wherein lignification is reduced in valve margin cells.

18. The plant of claim 13, wherein the promoter is a dehiscence zone-selective regulatory element.

20. (Amended) A method of delaying fruit dehiscence in a plant, the method comprising suppressing expression of an IND1 nucleic acid in the plant by introducing into the plant a recombinant expression cassette comprising a promoter operably linked to a polynucleotide encoding an IND1 polypeptide at least about 70% identical to SEQ ID NO: 2, wherein the IND1 polypeptide comprises a basic helix-loop-helix (bHLH) domain.

21. The method of claim 20, wherein the IND1 polypeptide comprises SEQ ID NO:2.

22. The method of claim 20, wherein the IND1 polynucleotide comprises positions from about 2765 to about 3361 of SEQ ID NO:1.

23. The method of claim 20, wherein the IND1 polynucleotide comprises SEQ ID NO:1.

24. (Amended) The method of claim 20, wherein the polynucleotide encoding the IND1 polypeptide is operably linked to the promoter in the antisense orientation.

25. (Amended) The method of claim 20, wherein the polynucleotide encoding the IND1 polypeptide is operably linked to the promoter in the sense orientation.

26. (Amended) The method of claim 25, wherein the polynucleotide further comprises a second polynucleotide sequence encoding the IND1 polypeptide wherein the second polynucleotide is operably linked to a second promoter in the antisense orientation.

27. The method of claim 20, wherein lignification is reduced in valve margin cells.

28. The method of claim 20, wherein the promoter is a dehiscence zone-selective regulatory element.

30. The method of claim 20, wherein the recombinant expression cassette is introduced into the plant using Agrobacterium.

34. (New) An expression cassette comprising a heterologous promoter operably linked to polynucleotide, or a complement thereof, wherein the polynucleotide is at least 65% identical to at least 200 contiguous nucleotides of SEQ ID NO:1, wherein introduction of the expression cassette into a plant to suppress IND1 expression results in a plant with delayed fruit dehiscence.

35. (New) The expression cassette of claim 34, wherein the polynucleotide is identical to at least 200 contiguous nucleotides of SEQ ID NO:1.

36. (New) The expression cassette of claim 34, wherein the polynucleotide is at least 500 nucleotides.

37. (New) The expression cassette of claim 34, wherein the polynucleotide is in a sense orientation with the promoter.

38. (New) The expression cassette of claim 34, wherein the promoter is constitutive.

39. The expression cassette of claim 34, wherein the promoter is tissue specific.

40. The expression cassette of claim 34, wherein the promoter is a dehiscence zone specific promoter.

41. (New) The method of claim 20, wherein the plant is a Brassica species.